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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/389,565	09/03/1999	DAVID M. NEVILLE, JR.	14028.0290	5574

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/389,565	NEVILLE, JR. ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-33,37-39 and 43-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *31-33,37 and 44-47* is/are allowed.

6)☐ Claim(s) *30,38,39,43 and 48-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 30-33, 37-39, 43-48, and newly added Claim 49-51, are pending and being acted upon.

2. Applicant's amendment and remarks, filed 1/06/06, are acknowledged. In view of Applicant's amendment, the previous rejections of Claims 32 and 33 under the first paragraph of 35 U.S.C. 112 for the recitation of an "optional" linker have been withdrawn.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 30, 38, 39, and 43, and newly added Claims 49-51 stand/are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) In Claim 30, a fusion immunotoxin comprising … a diphtheria toxin moiety … wherein 152-145 carboxy terminal amino acid residues are truncated from the native diphtheria toxin moiety, and,

B) In Claims 38 and 43 (and newly added Claim 50), a method for inhibiting rejection of transplanted tissue or organs in a subject,

are not supported by the specification.

C) The immunotoxin of Claim 48 comprising a "truncated toxin moiety not recognized by inhibitory anti-diphtheria toxin antibodies" is not disclosed in the specification.

Regarding A), Applicant argues that the disclosure of mutants DT390, DT383, and MSPΔ5 support the claim. Applicant further argues that these mutants represent both ends of the claimed range as well as an example with the range. Applicant argues that the claimed intermediate truncations would have the same function as the disclosed species and that they are not unpredictable. Applicant further argues that each species within the claimed range need not be described.

First note that Applicant's arguments regarding function and unpredictability are not relevant to the instant rejection. The instant rejection is not for lack of

enablement, but rather for lack of adequate written description. Regarding the rejection for lack of adequate written description, if Applicant had chosen to disclose the claimed range in the instant specification there would be no rejection here. The fact that Applicant disclosed 3 of the 8 species that would fall within the claimed range does not demonstrate that Applicant envisioned the entire range, and all of the species within it, at the time of filing.

It is the Examiner's position that it is well-established that the requirement of the first paragraph of 35 U.S.C. 112 is not satisfied by subject matter that is not disclosed. but might be obvious. One shows possession of an invention by describing the invention, including all claimed limitations. *Lockwood v. American Airlines*, 1966, 41 USPQ2d 1961 (CAFC 1997), makes clear "all the limitations must appear in the specification".

Regarding B), Applicant argues that support for "inhibiting rejection of transplanted tissue or organs" can be found at page 31, lines 17-19; page 32, lines 19-26; page 40, lines 3-7; and page 39, lines 33-35 of the specification.

A review of the specification shows that 3 of the cites concern allo-skin grafts in monkeys, and the other cite concerns "mismatched" kidney transplants.

It is the Examiner's position that these minimal disclosures do not adequately describe the entire genus of transplanted tissue or organs for which rejection might be inhibited. The claims encompass the inhibition of rejection in *any* species, while only rhesus monkey is disclosed, and *any* type of tissue or organ, while only skin and kidney are disclosed, and then only minimally. For example, the cite at page 40 of the specification discloses only, "FN18-CRM9 has also been used as an adjunct in inducing tolerance to mismatched kidney transplants (24)". Reference 24, Parlevliet et al., 1992, comprises a review of the use of OKT3 (not the antibody of the instant claims or specification) for the inhibition of kidney rejection. This disclosure cannot be considered even adequate for the use of the scFv antibody of the claims in methods of inhibiting kidney transplantation alone, much less for the inhibition of rejection in all of the other tissue and organ types encompassed by the claims.

Regarding C), Applicant indicates that support for the new amendment can be found in original Claims 1 and 3 and at pages 40, 48, and 49 of the specification. None of these cites teach the limitation set forth above in the context of the scFv of the instant claim. Page 40 discloses that a truncation mutant was made, and pages 48 and 49 disclose MSPΔ5 and a DT-390 construct, respectively. No generic scFv as set forth in the rejection above is disclosed.

Applicant's arguments, filed 1/06/06 have been fully considered but they are not persuasive.

In support of Claim 48, Applicant now cites original Claims 1 and 4-7.

None of these claims recite the limitation of a "truncated toxin moiety not recognized by inhibitory anti-diphtheria toxin antibodies".

In support of Claims 38, 43, and new Claim 50, Applicant notes that the claims are now limited to inhibiting the rejection of mismatched kidney and cites pages 27, 39, and 40 of the specification.

Applicant is advised that these cites disclose only the use of the non-human primate FN18-CRM9 antibody and then only as an adjunct for inducing tolerance in mismatched kidney transplantation. They do not disclose the generic method of the claims employing a UCHT1-diphtheria immunotoxin to inhibit transplant rejection (which does not necessarily encompass the induction of tolerance).

Applicant makes several arguments, e.g., "Applicants respectfully remind the Examiner that there is no *per se* rule requiring human data", and "One of skill in the art would also clearly know that experiments in monkeys using FN18 are representative of the use of UCHTI in humans", that might be relevant to an enablement rejection but have no bearing on the instant rejections for a lack of adequate written description for the introduction of new matter into the claims.

Applicant asserts, "One of skill in the art would recognize that a description of a 152 carboxy terminal truncation mutant literally encompasses (i.e., discloses) a 145 amino acid truncation mutant, a 146 amino acid truncation mutant, a 147 amino acid truncation mutant, a 148 amino acid truncation mutant, a 149 amino acid truncation mutant, a 150 amino acid truncation mutant, a 151 amino acid truncation mutant, and a 152 amino acid truncation mutant. This is because the possession of a 152 amino acid truncation mutant necessarily comprises a 1, 10, 20, 30, 40, 100, 125, 145, 146, 147, 148, 149, 150, 151, and 152 amino acid truncation, as well as, any other truncation between 1 and 152 amino acids".

The logic of this argument is not readily apparent to the Examiner. Employing the logic of the argument, it would appear that possession of a whole product would provide support for *any* piece or portion of any product. Such is clearly not the case.

Applicant argues, "Given the nature of the element at issue, a truncation, the skilled person would recognize from the disclosure of the longest and shortest truncation that all truncations encompassed by the longest and shortest truncation (i.e., the range "152-145") are in applicants' possession".

The Examiner disagrees for the reasons set forth above.

Applicant asserts, "Although applicants range does not represent a genus, but rather a defined set of species, arguments regarding written description of a genus are not required. However, because some aspects of the present rejection suggest that the range could be viewed as a genus and rejections made along those lines, a response on that issue is provided".

Again, the logic of this argument is not readily apparent to the Examiner.

Applicant argues that the specification discloses 3 of the 8 species comprising the claimed genus.

This argument seems to contradict the argument set forth earlier in the same paragraph that "applicants range does not represent a genus"? Regardless, it remains the Examiner's position that the disclosure is insufficient.

Applicant cites Examples 16 and 13 in the Revised Interim Written Description Guidelines Training Materials.

Example 16 of the Revised Interim Written Description Guidelines Training Materials teaches that claims drawn to a polyclonal antibody that binds a well-characterized protein are adequately described. The Guidelines are silent regarding whether or not specific recombinant truncation mutant constructs would be adequately described. Example 13 teaches a protein variant which was not adequately described. It is unclear how citing an example in which a protein comprising substitutions, deletions, subtractions, and additions, was not adequately described, demonstrates an adequate written description for the specific recombinant truncation mutant constructs of the instant claims.

5. Claims 31-33, 37 and 44-47 are allowed.

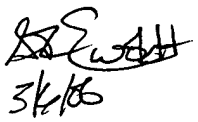
6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

8. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.



3/6/06

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